

Voluntary Worldwide Withdrawal of VIOXX® (rofecoxib)



Merck & Co Inc, announced at the end of September 2004 a voluntary worldwide withdrawal of VIOXX® (rofecoxib), its arthritis and acute pain medication. The company's decision, which is effective immediately, is based on new, three-year data from a prospective, randomized, placebo-controlled clinical trial, the APPROVe (Adenomatous Polyp Prevention on VIOXX) trial.

The trial, which is being stopped, was designed to evaluate the efficacy of VIOXX 25 mg in preventing recurrence of colorectal polyps in patients with a history of colorectal adenomas. In this study, there was an increased relative risk for confirmed cardiovascular events, such as heart attack and stroke, beginning after 18 months of treatment in the patients taking VIOXX compared to those taking placebo. The results for the first 18 months of the APPROVe study did not show any increased risk of confirmed cardiovascular events on VIOXX, and in this respect, are similar to the results of two placebo-controlled studies described in the current U.S. labeling for VIOXX.

"We are taking this action because we believe it best serves

the interests of patients," said Raymond V. Gilmartin, chairman, president and chief executive officer of Merck. "Although we believe it would have been possible to continue to market VIOXX with labeling that would incorporate these new data, given the availability of alternative therapies, and the questions raised by the data, we concluded that a voluntary withdrawal is the responsible course to take."

APPROVe was a multi-center, randomized, placebo-controlled, double-blind study to determine the effect of 156 weeks (three years) of treatment with VIOXX on the recurrence of neoplastic polyps of the large bowel in patients with a history of colorectal adenoma. The trial enrolled 2,600 patients and compared VIOXX 25 mg to placebo. The trial began enrollment in 2000.

Results of the VIGOR (VIOXX Gastrointestinal Outcomes Research) study, released in March 2000, demonstrated that the risk of gastrointestinal toxicity with VIOXX was less than with naproxen, but indicated an increased risk of cardiovascular events versus naproxen. However, in other studies including Merck's Phase III studies that were the basis of regulatory approval of the product, there was not an increased risk of cardiovas-

cular events with VIOXX compared with placebo or VIOXX compared with other non-naproxen non-steroidal anti-inflammatory drugs (NSAIDs). Merck began long-term randomized clinical trials to provide an even more comprehensive picture of the cardiovascular safety profile of VIOXX.

"Merck has always believed that prospective, randomized, controlled clinical trials are the best way to evaluate the safety of medicines. APPROVe is precisely this type of study - and it has provided us with new data on the cardiovascular profile of VIOXX," said Peter S. Kim, Ph.D., president of Merck Research Laboratories. "While the cause of these results is uncertain at this time, they suggest an increased risk of confirmed cardiovascular events beginning after 18 months of continuous therapy. While we recognize that VIOXX benefited many patients, we believe this action is appropriate."

The results of clinical studies with one molecule in a given class are not necessarily applicable to others in the class. Therefore, the clinical significance of the APPROVe trial, if any, for the long-term use of other drugs in this class, consisting of COX-2 specific inhibitors and NSAIDs, is unknown. The company will work with regulatory authorities in the 47 countries where ARCOXIA is approved to assess whether changes to the prescribing information for this class of drugs, including ARCOXIA, are warranted.

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